

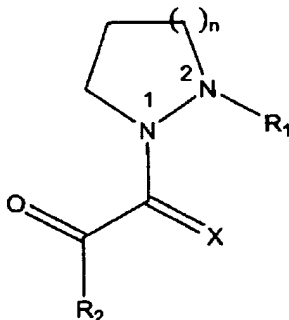
Application. No. 09/835,523
Atty. Dkt. No. 054707-0661
Response To Final Office Action Of 03-25-2005

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended) A compound of formula I



I

~~or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:~~

or a pharmaceutically acceptable salt or ester thereof, wherein:

n = 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, and -CONR₃CN;

R₂ is selected from the group consisting of hydrogen, C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from R₃;

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl,

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C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, ~~thiocarbonyl~~, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, ~~carbonyl~~, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S,

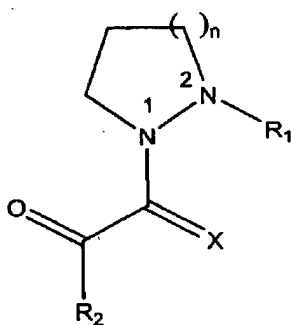
wherein the heteroaryl, carbocycle, and heterocycle are selected from cyclopentyl, cyclohexyl, cycloheptyl, phenyl, benzyl, naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, indolyl, isoindolyl, indolinyl, benzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, benzthiazolyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, pyrrolyl, pyrrolidinyl, pyridinyl, pyrimidinyl, purinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, quinolizinyl, furyl, thiophenyl, imidazolyl, oxazolyl, benzoxazolyl, thiazolyl, isoxazolyl, isotriazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, trithianyl, indolizinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, thienyl, tetrahydroisoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, adamantyl, pyrrole groups, thiophene groups, pyridine groups, and isoxazole groups.

2. (Original) The compound of claim 1, wherein the compound is non-immunosuppressive.

3. (Currently Amended) The compound of claim 1, wherein said compound is selected from the group consisting of:

- 3, 3-dimethyl-N-[2-(5-phenylpentanoyl)-tetrahydro-1H-1-pyrazolyl]-1,2-pentanedione;
- 3, 3-dimethyl-N-[2-(3-phenylpropanoyl)-tetrahydro-1H-1-pyrazolyl]-1,2-pentanedione;
- 3, 3-dimethyl-1-[2-(5-(3-pyridyl) pent-4-ynoyl)-pyrazolidinyl]pentane-1, 2-dione;
- 3, 3-dimethyl-1-[2-(5-(cyano) pent-4-ynoyl)pyrazolidinyl]-pentane-1, 2-dione;
- 3, 3-dimethyl-1-[2-(4-phenylbutanoyl) pyrazolidinyl]-pentane-1, 2-dione;
- 3, 3-dimethyl-1-[2-(6-phenylhexanoyl) pyrazolidinyl]-pentane-1, 2-dione;

4. (Currently Amended) A pharmaceutical composition comprising:
(i) a therapeutically effective amount of a compound of formula I:



I

~~or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:~~

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or a pharmaceutically acceptable salt or ester thereof, wherein:

n = 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, and -CONR₃CN;

R₂ is selected from the group consisting of hydrogen, C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from R₃;

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, ~~thiocarbonyl~~, ~~thiocarbonyl~~, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, ~~carbonyl~~, cyano, nitro, imino, sulfonyl, ~~thiocarbonyl~~, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S; and

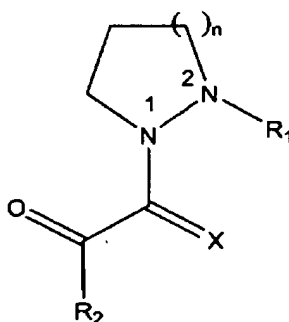
(ii) a pharmaceutically acceptable carrier,

wherein the heteroaryl, carbocycle, and heterocycle are selected from cyclopentyl, cyclohexyl, cycloheptyl, phenyl, benzyl, naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, indolyl, isoindolyl, indolinyl, benzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, benzthiazolyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, pyrrolyl, pyrrolidinyl, pyridinyl, pyrimidinyl, purinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, quinoliziny, furyl, thiophenyl, imidazolyl, oxazolyl, benzoxazolyl, thiazolyl, isoxazolyl, isotriazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, trithianyl, indoliziny, pyrazolyl, pyrazolinyl, pyrazolidinyl, thienyl, tetrahydroisoquinolinyl, cinnolinyl, phthalazinyl,

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quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, adamantyl, pyrrole groups, thiophene groups, pyridine groups, and isoxazole groups.

5. (Withdrawn) The pharmaceutical composition of claim 4, further comprising an additional neurotrophic factor.
6. (Withdrawn) The pharmaceutical composition of claim 5, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, cilia neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.
7. (Currently Amended) A method for treating peripheral neuropathy, Alzheimer's disease, Parkinson's disease, Huntington's disease, or amyotrophic lateral sclerosis affecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula I:



I

~~or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:~~
or a pharmaceutically acceptable salt or ester thereof, wherein:

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$n = 1-3$;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, $-COOH$, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, $-CN$, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, and $-CONR_3CN$;

R_2 is selected from the group consisting of hydrogen, C_1 - C_9 straight or branched chain alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from R_3 ;

R_3 is selected from the group consisting of hydrogen, C_1 - C_9 alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1 - C_9 thioalkyl, C_2 - C_9 thioalkenyl, C_1 - C_9 alkylamino, C_2 - C_9 alkenylamino, cyano, nitro, imino, sulfonyl, ~~thiocarbonyl~~, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, ~~carbonyl~~, cyano, nitro, imino, sulfonyl, ~~thiocarbonyl~~, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S,

wherein the heteroaryl, carbocycle, and heterocycle are selected from cyclopentyl, cyclohexyl, cycloheptyl, phenyl, benzyl, naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, indolyl, isoindolyl, indolinyl, benzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, benzthiazolyl, tetrahydrofuranyl, tetrahydropyranyl, pyridyl, pyrrolyl, pyrrolidinyl, pyridinyl, pyrimidinyl, purinyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, quinoliziny, furyl, thiophenyl, imidazolyl, oxazolyl, benzoxazolyl, thiazolyl, isoxazolyl, isotriazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, trithianyl, indoliziny, pyrazolyl, pyrazolinyl, pyrazolidinyl, thienyl, tetrahydroisoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazoyl, acridinyl, phenazinyl,

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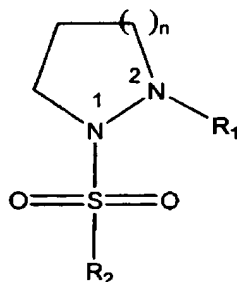
phenothiazinyl, phenoxazinyl, adamantyl, pyrrole groups, thiophene groups, pyridine groups, and isoxazole groups.

8. (Currently Amended) The method of claim 7, wherein the method is for treating peripheral neuropathy ~~neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.~~

9. (Currently Amended) The method of claim 8, wherein the ~~method is for treating neurological disorder is selected from the group consisting of peripheral neuropathy is~~ caused by physical injury or disease state, ~~traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.~~

10. (Currently Amended) The method of claim 7 9, wherein the method is for treating neurological disorder relating to neurodegeneration ~~is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and or amyotrophic lateral sclerosis.~~

11. (Withdrawn) A compound of formula II:



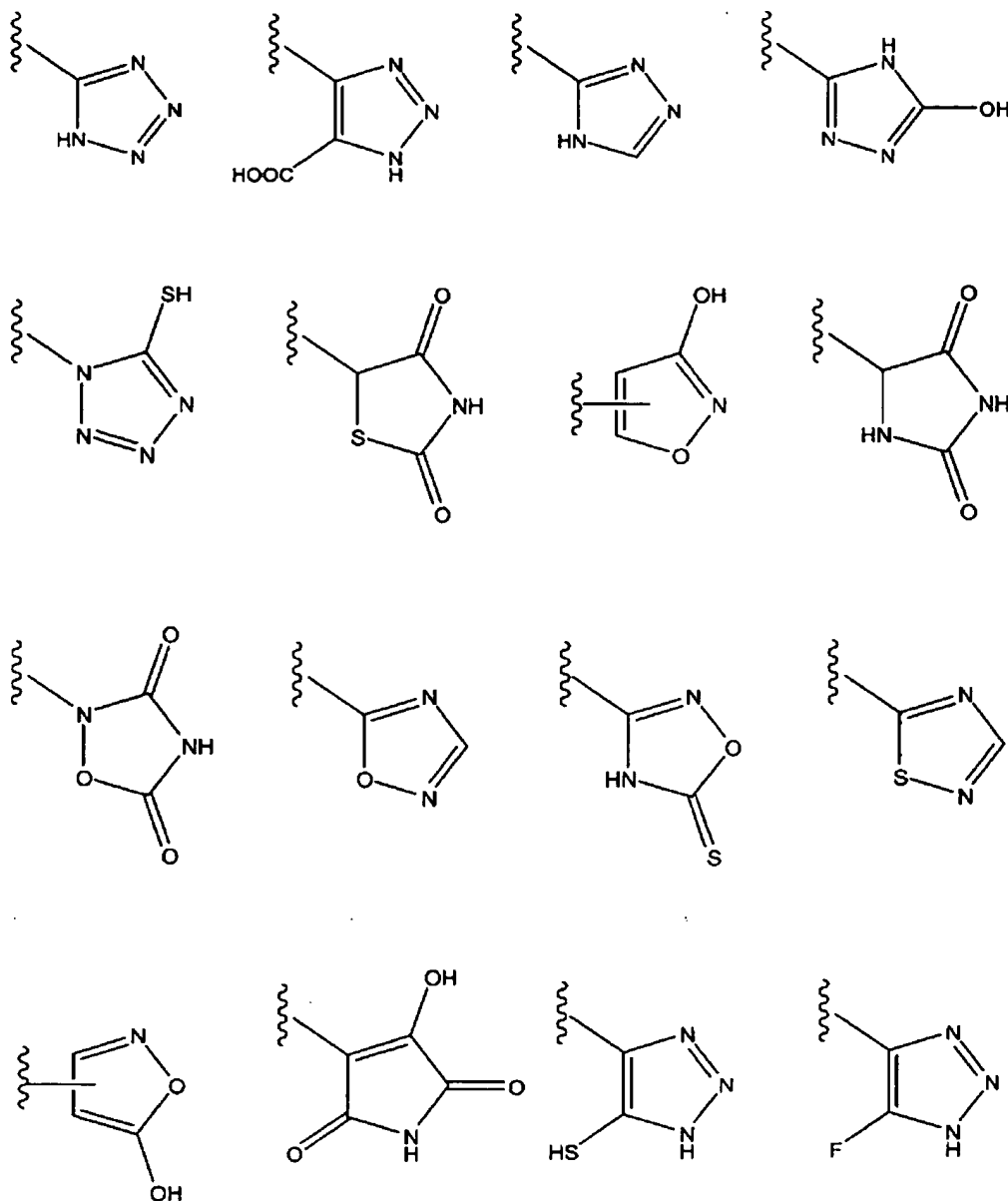
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or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

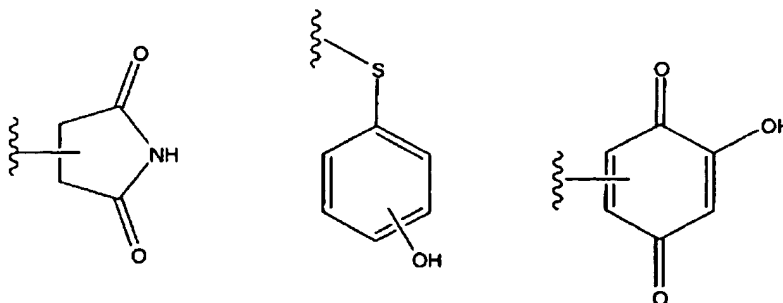
n = 1-3;

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R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, $-COOH$, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, $-CN$, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,



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wherein said R₁ group is either unsubstituted or additionally substituted with R₃;

R₂ is selected from the group consisting of hydrogen, C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R₃;

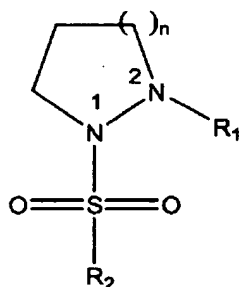
R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

12. (Withdrawn) The compound of claim 11, wherein the compound is non-immunosuppressive.

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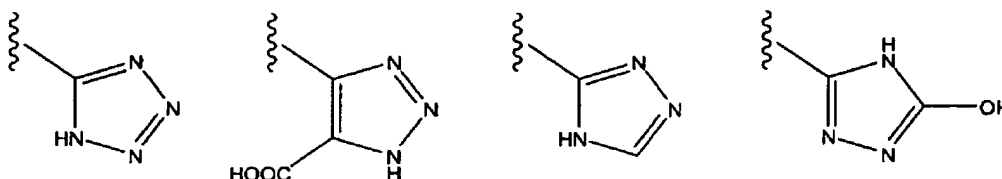
13. (Withdrawn) The compound of claim 11, which is selected from the group consisting of:
3-phenylpropyl 2-[benzylsulfonyl] pyrazolidine-carboxylate;
4-phenylbutyl 2-[benzylsulfonyl] perhydropyridazine-carboxylate;
1-(5-phenylpentanoyl)-2-(benzylsulfonyl) tetrahydro-1H-1-pyrazole; and
pharmaceutically acceptable salts, esters and solvates thereof.
14. (Withdrawn) A pharmaceutical composition comprising:
(i) a therapeutically effective amount of a compound of formula II:



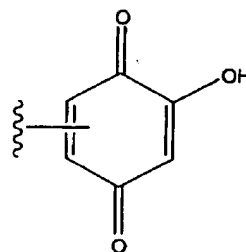
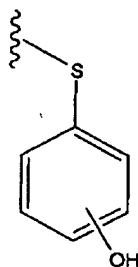
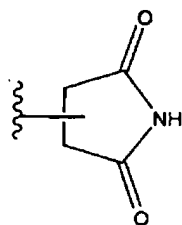
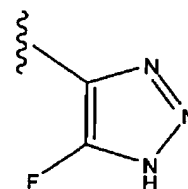
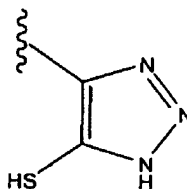
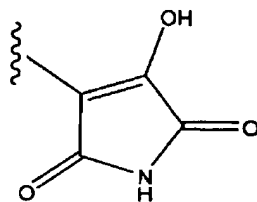
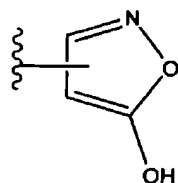
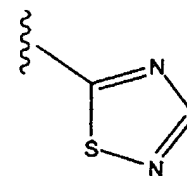
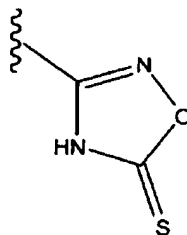
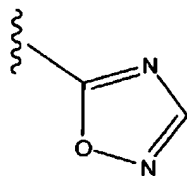
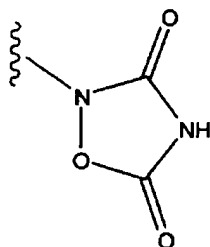
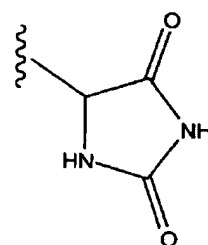
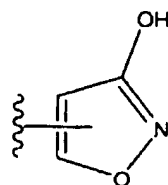
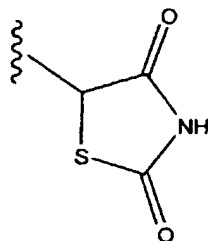
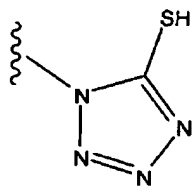
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n = 1-3$;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, $-COOH$, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, $-CN$, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,



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wherein said R₁ group is either unsubstituted or additionally substituted with R₃;

R₂ is selected from the group consisting of hydrogen, C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R₃;

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

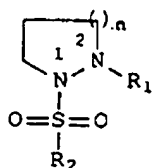
(ii) a pharmaceutically acceptable carrier.

15. (Withdrawn) The pharmaceutical composition of claim 14, further comprising an additional neurotrophic factor.

16. (Withdrawn) The pharmaceutical composition of claim 15, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

17. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula II:

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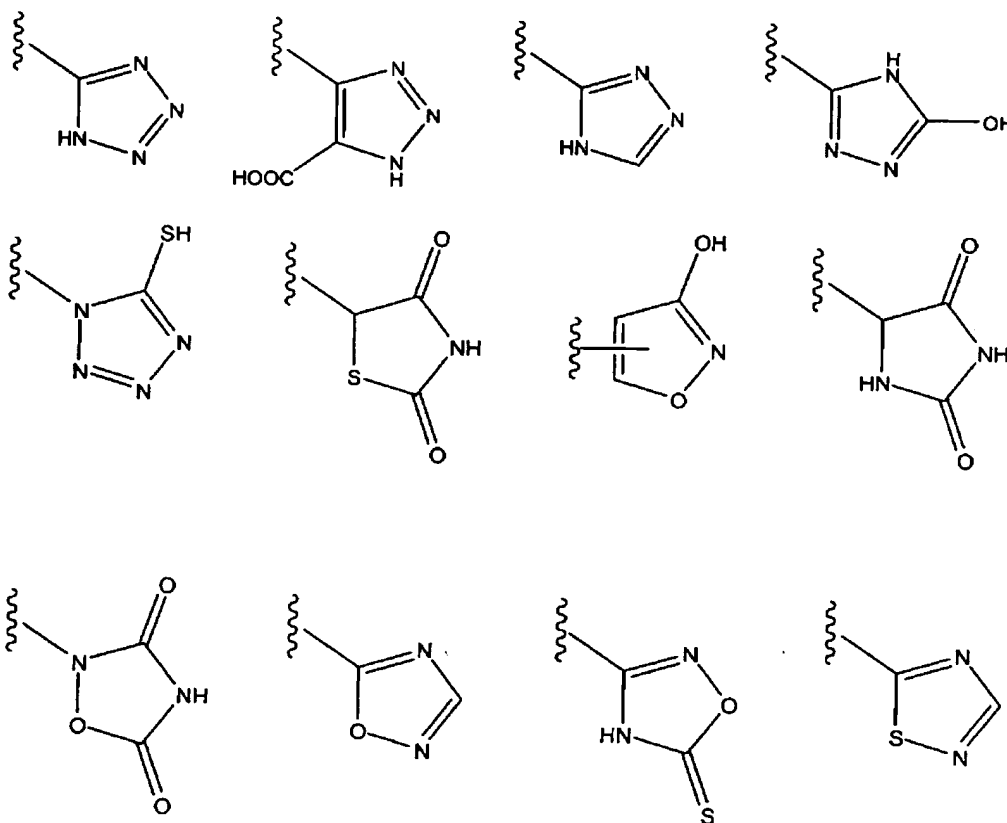


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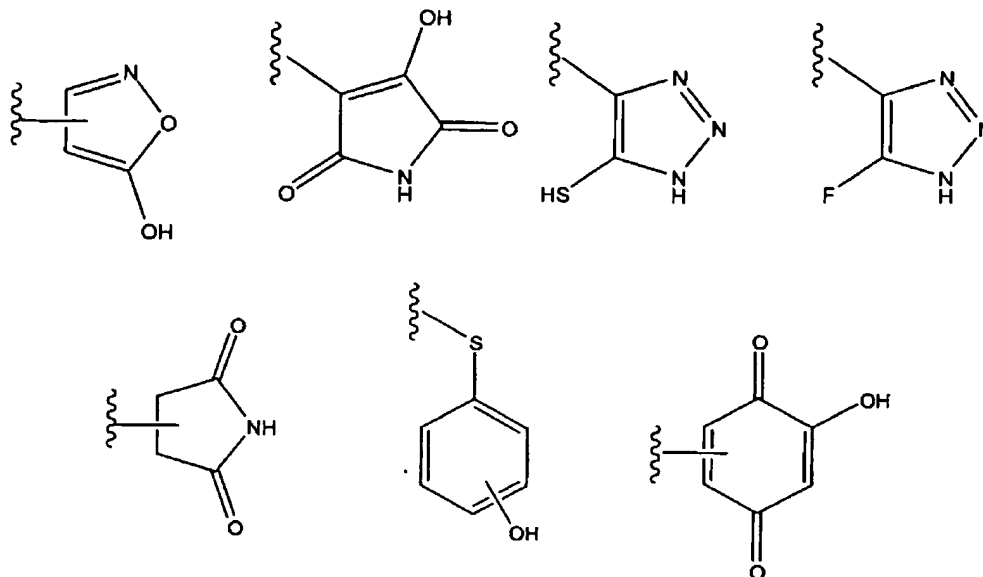
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,



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wherein said R_1 group is either unsubstituted or additionally substituted with R_3 ;

R_2 is selected from the group consisting of hydrogen, C_1 - C_9 straight or branched chain alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R_3 ; and

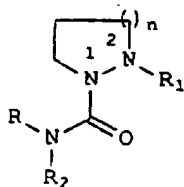
R_3 is selected from the group consisting of hydrogen, C_1 - C_9 alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1 - C_9 thioalkyl, C_2 - C_9 thioalkenyl, C_1 - C_9 alkylamino, C_2 - C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulphydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl,

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cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

18. (Withdrawn) The method of claim 17, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.
19. (Withdrawn) The method of claim 18, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.
20. (Withdrawn) The method of claim 19, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.
21. (Withdrawn) A compound of formula III:



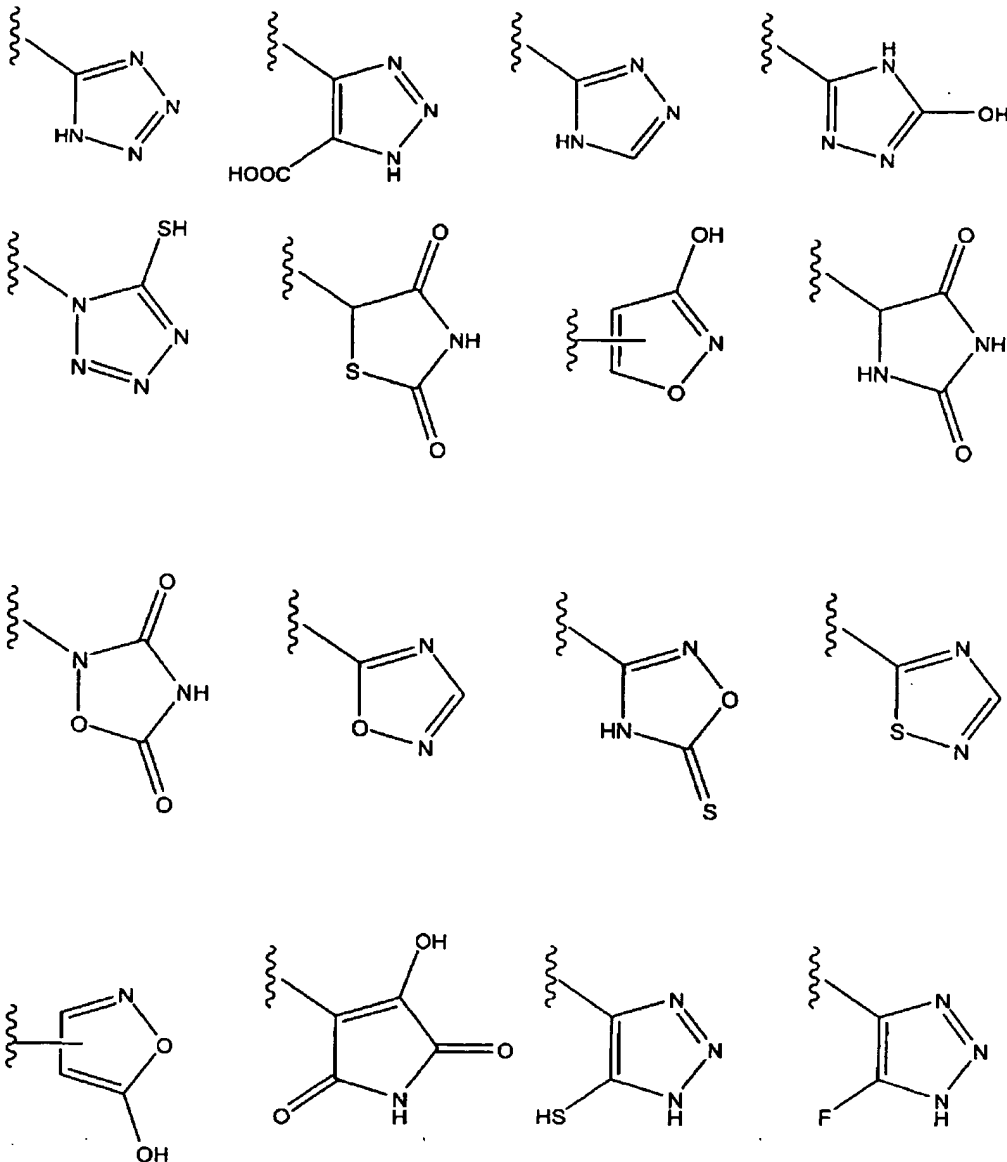
III

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

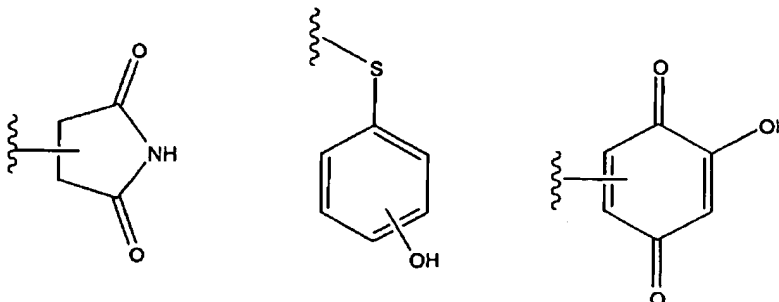
n is 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,

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wherein said R₁ group is either unsubstituted or additionally substituted with R₃;

R and R₂ are independently C₁-C₉ alkyl, C₂-C₉ alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s) selected from R₃; and

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

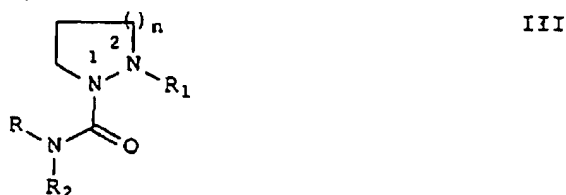
wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

22. (Withdrawn) The compound of claim 21, wherein the compound is non-immunosuppressive.

23. (Withdrawn) The compound of claim 21, wherein said compound is 1-(5-phenylpentanoyl)-2-(N,N-dicyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole or a pharmaceutically acceptable salt, ester or solvate thereof.

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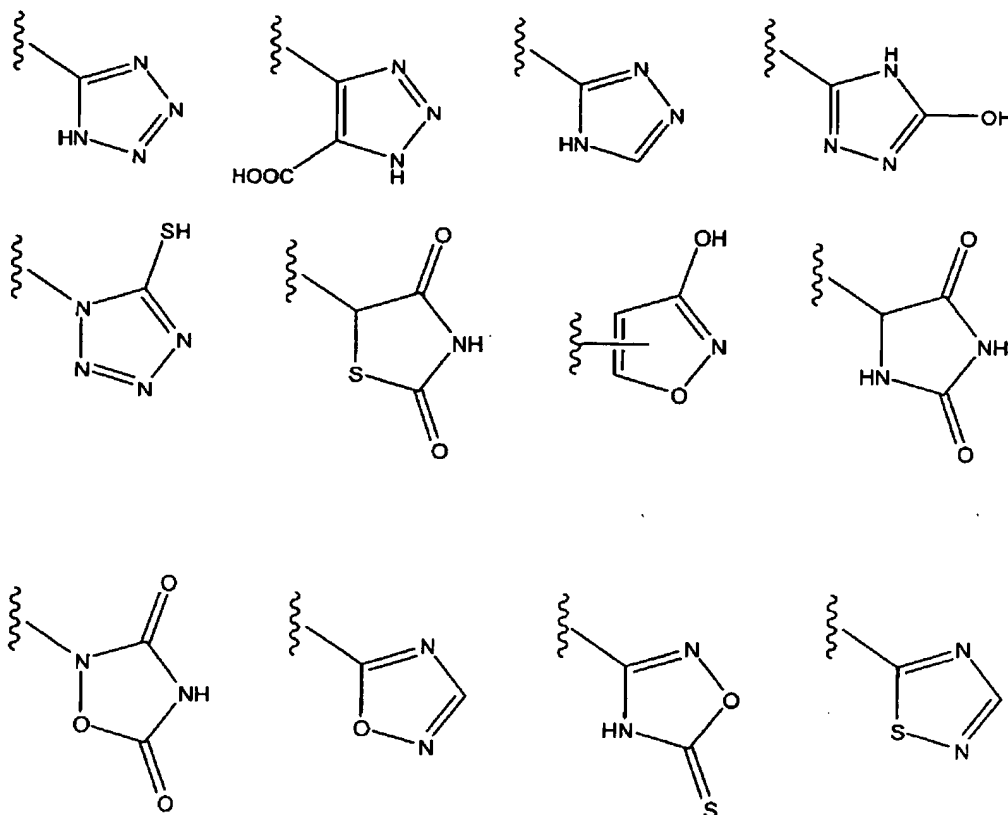
24. (Withdrawn) A pharmaceutical composition comprising:
(i) a therapeutically effective amount of a compound of formula III:



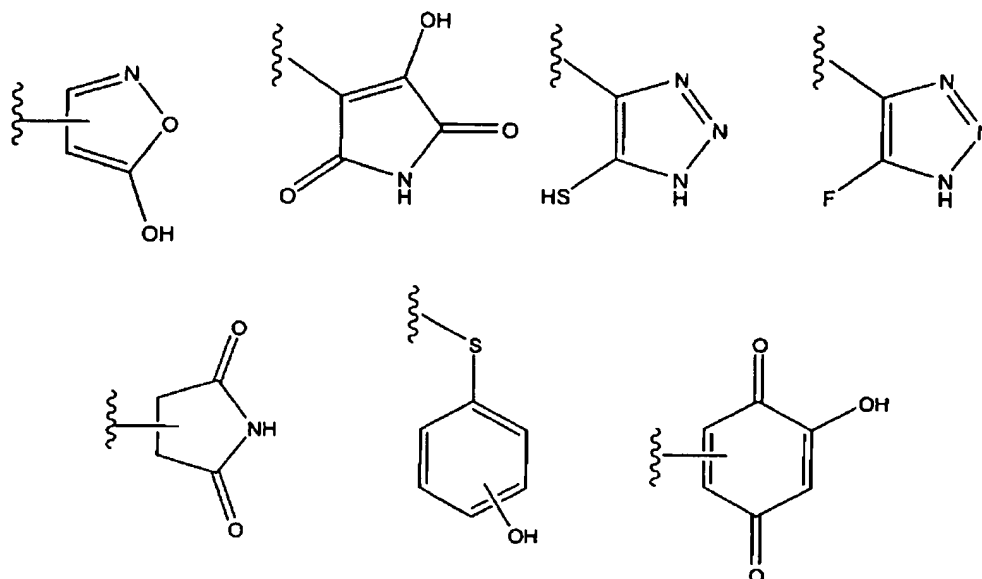
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, $-COOH$, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, $-CN$, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,



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wherein said R_1 group is either unsubstituted or additionally substituted with R_3 ;

R and R_2 are independently C_1 - C_9 alkyl, C_2 - C_9 alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s) selected from R_3 ; and

R_3 is selected from the group consisting of hydrogen, C_1 - C_9 alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1 - C_9 thioalkyl, C_2 - C_9 thioalkenyl, C_1 - C_9 alkylamino, C_2 - C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

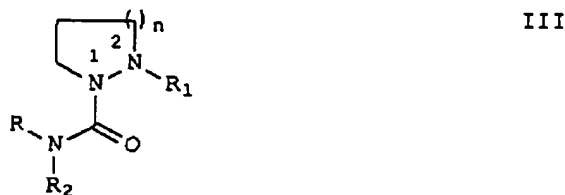
(ii) a pharmaceutically acceptable carrier.

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25. (Withdrawn) The pharmaceutical composition of claim 24, further comprising an additional neurotrophic factor.

26. (Withdrawn) The pharmaceutical composition of claim 25, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

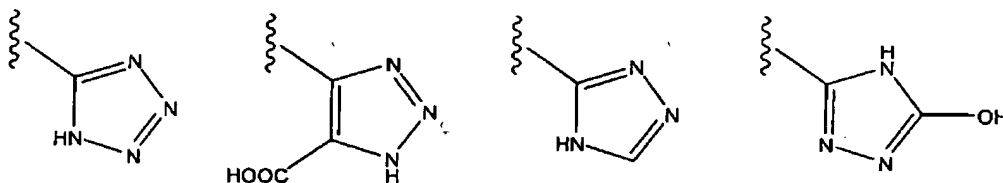
27. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula III:



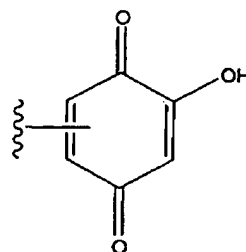
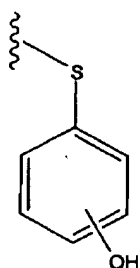
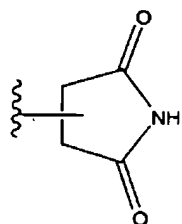
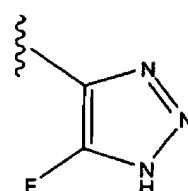
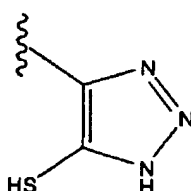
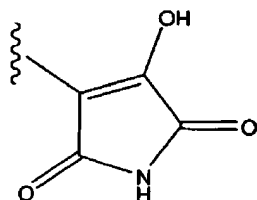
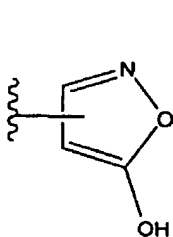
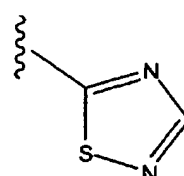
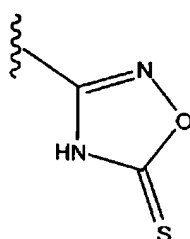
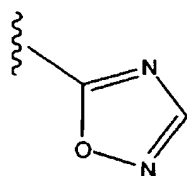
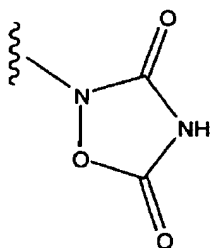
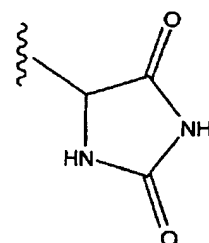
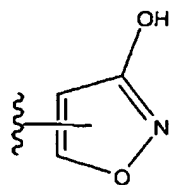
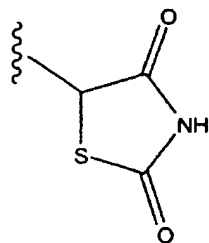
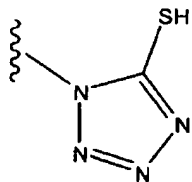
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,



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wherein said R₁ group is either unsubstituted or substituted with one or more substituent(s);

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R and R₂ are independently C₁-C₉ alkyl, C₂-C₉ alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s); and

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, , nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

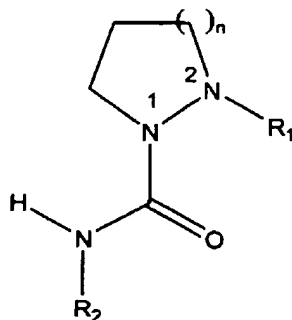
28. (Withdrawn) The method of claim 27, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

29. (Withdrawn) The method of claim 28, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

30. (Withdrawn) The method of claim 29, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

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31. (Withdrawn) A compound of formula IV:

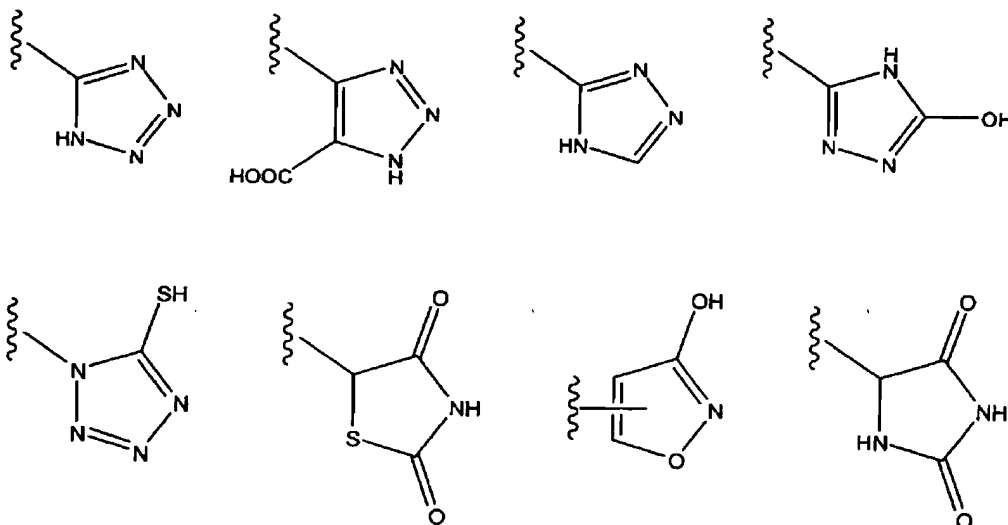


IV

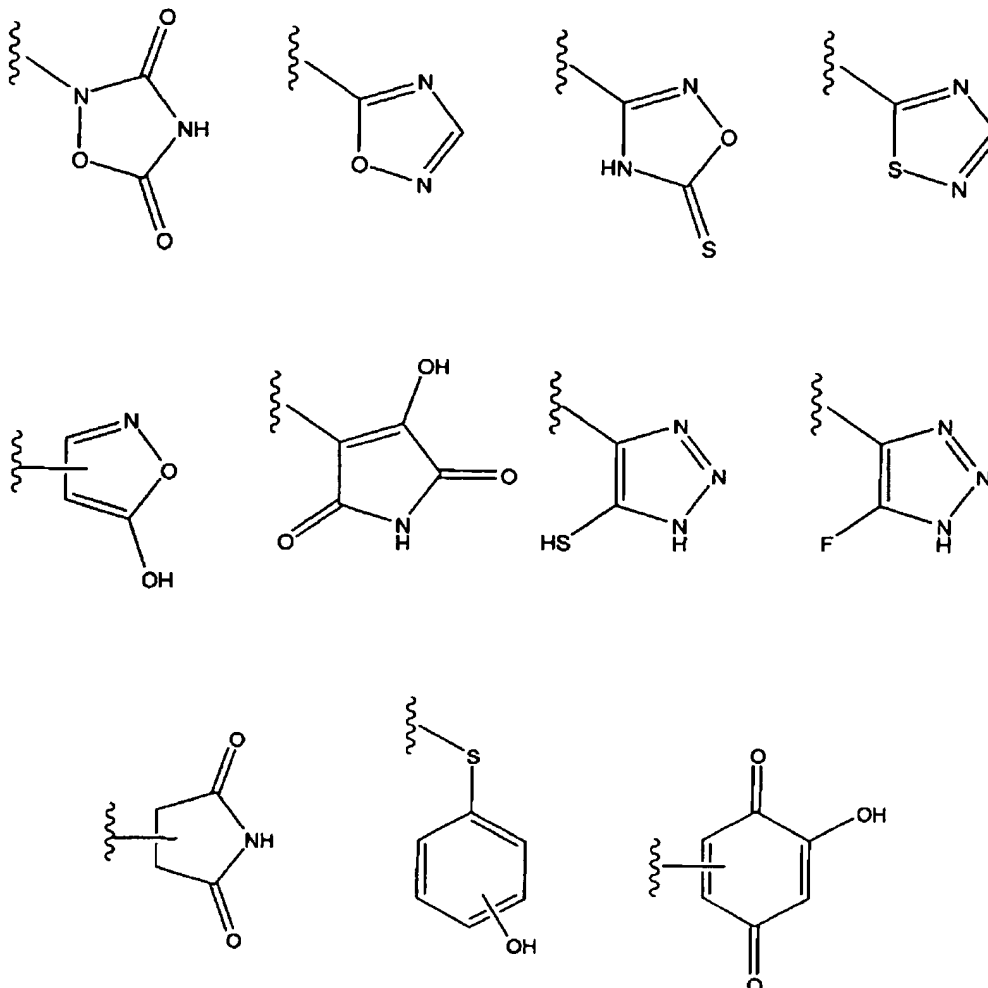
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,



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wherein said R_1 group is either unsubstituted or additionally substituted with R_3 ; and

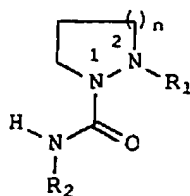
R_2 is C_1 - C_9 alkyl, C_2 - C_9 alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from R_3 ; and

R_3 is selected from the group consisting of hydrogen, C_1 - C_9 alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1 - C_9 thioalkyl, C_2 - C_9 thioalkenyl,

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C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

32. (Withdrawn) The compound of claim 31, wherein the compound is non-immunosuppressive.
33. (Withdrawn) The compound of claim 31, wherein said compound is selected from the group consisting of:
- 3-phenylpropyl 2-(N-cyclohexylcarbamoyl) pyrazolidine-carboxylate;
 - 4-phenylbutyl 2-(N-cyclohexylcarbamoyl) perhydro-pyridazinecarboxylate;
 - 1-(5-phenylpentanoyl)-2-(N-cyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole; and
 - pharmaceutically acceptable salts, esters and solvates thereof.
34. (Withdrawn) A pharmaceutical composition comprising:
- (i) a therapeutically effective amount of a compound of formula IV:

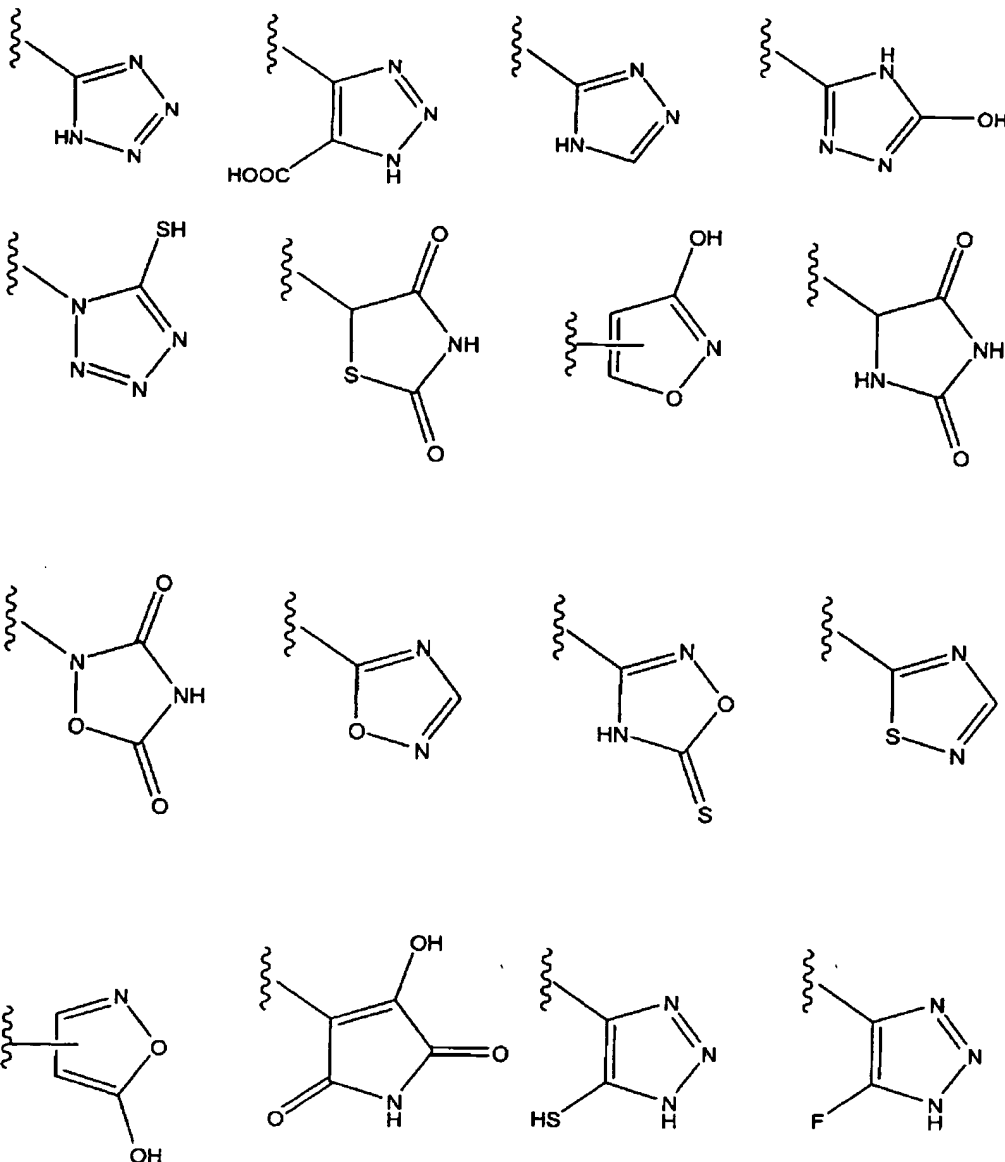


IV

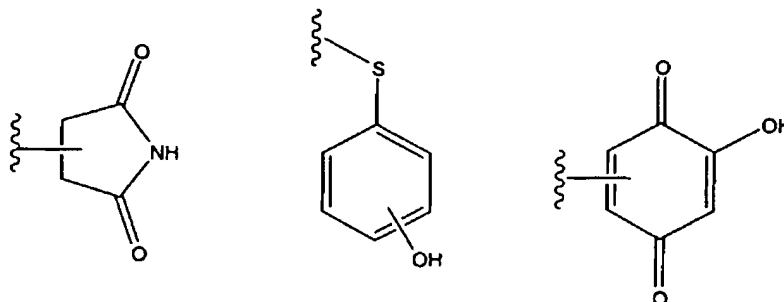
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:
n is 1-3;

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R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, -CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,



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wherein said R₁ group is either unsubstituted or additionally substituted with R₃; and

R₂ is C₁-C₉ alkyl, C₂-C₉ alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from R₃; and

R₃ is selected from the group consisting of hydrogen, C₁-C₉ alkyl, C₂-C₉ straight or branched chain alkenyl, C₂-C₉ straight or branched chain alkynyl, C₁-C₉ alkoxy, C₂-C₉ alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C₁-C₉ thioalkyl, C₂-C₉ thioalkenyl, C₁-C₉ alkylamino, C₂-C₉ alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

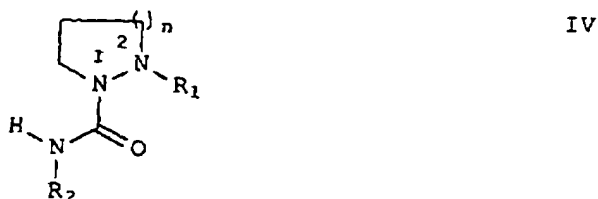
35. (Withdrawn) The pharmaceutical composition of claim 34, further comprising an additional neurotrophic factor.

36. (Withdrawn) The pharmaceutical composition of claim 35, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor,

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acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

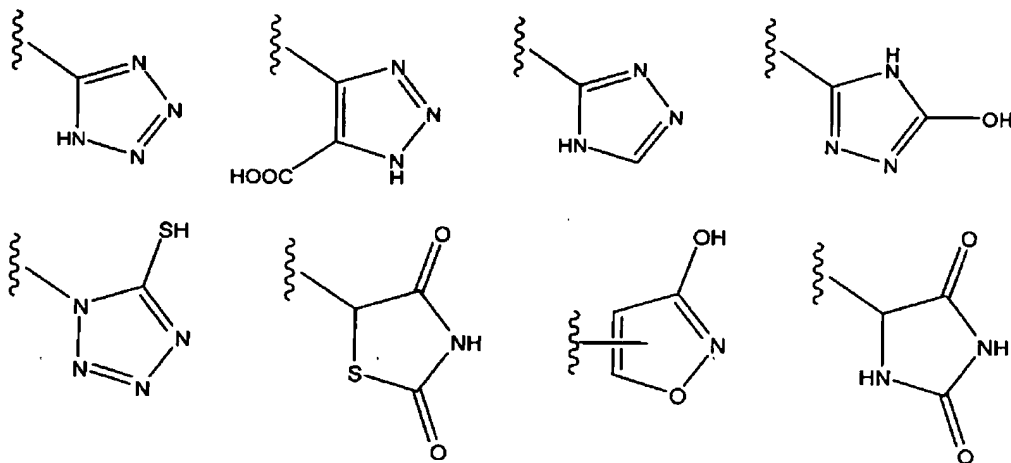
37. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula IV:



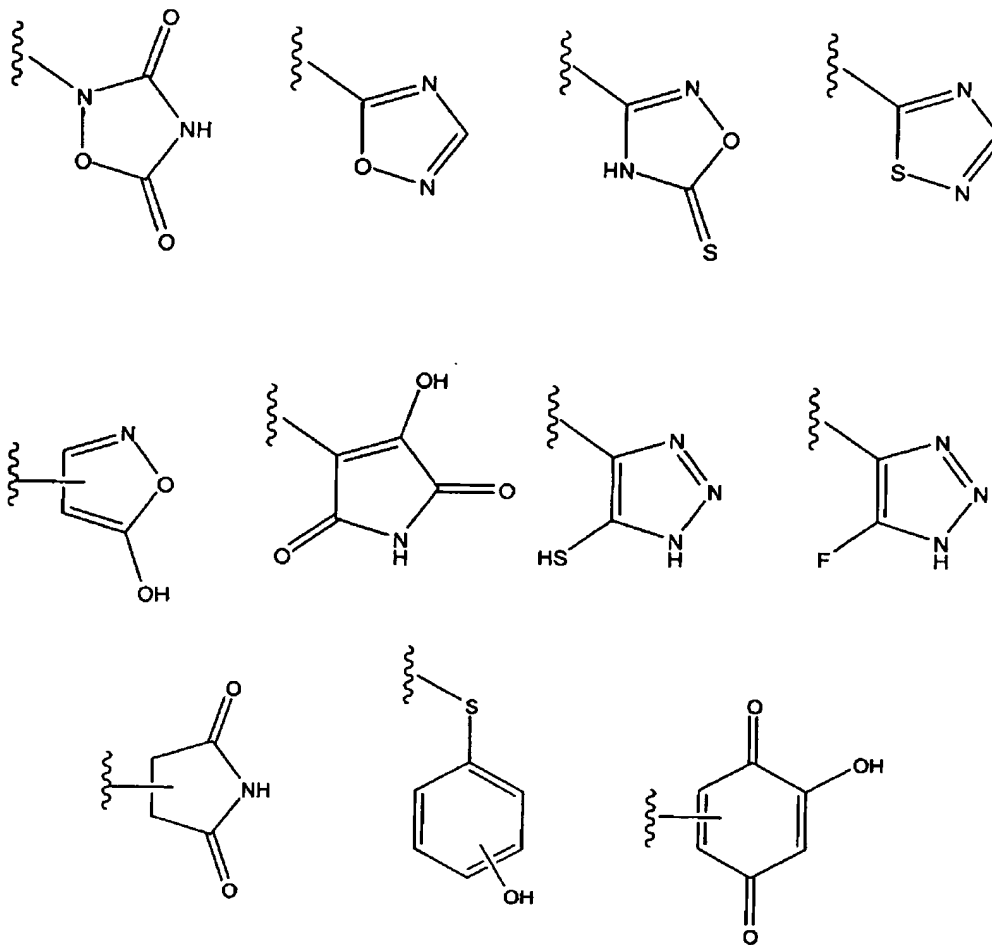
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R₁ is selected from the group consisting of -CR₃, -COOR₃, -COR₃, -COOH, -SO₃H, -SO₂HNR₃, -PO₂(R₃)₂, CN, -PO₃(R₃)₂, -OR₃, -SR₃, -NHCOR₃, -N(R₃)₂, -CON(R₃)₂, -CONH(O)R₃, -CONHNHSO₂R₃, -COHNSO₂R₃, -CONR₃CN,



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wherein said R_1 group is either unsubstituted or additionally substituted with R_3 ; and

R_2 is C_1 - C_9 alkyl, C_2 - C_9 alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from R_3 ; and

R_3 is selected from the group consisting of hydrogen, C_1 - C_9 alkyl, C_2 - C_9 straight or branched chain alkenyl, C_2 - C_9 straight or branched chain alkynyl, C_1 - C_9 alkoxy, C_2 - C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1 - C_9 thioalkyl, C_2 - C_9 thioalkenyl, C_1 - C_9 alkylamino, C_2 - C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

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wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

38. (Withdrawn) The method of claim 37, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of a neurological disorder.

39. (Withdrawn) The method of claim 38, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

40. (Withdrawn) The method of claim 39, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis.

41-47. (Canceled)

48. (Previously Presented) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 1.

49. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 11.

50. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 21.

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51. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 31.